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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,217	03/04/2002	Yong Yao	053735-5004-01	2158

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EXAMINER

ULM, JOHN D

ART UNIT PAPER NUMBER

1646

DATE MAILED: 06/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,217	YAO ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 05 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-102 is/are pending in the application.
- 4a) Of the above claim(s) 14 and 86-102 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-13 and 15-85 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>11/03,06/03,7/02,11/02</u> | 6) <input type="checkbox"/> Other: _____ |

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- 1) Claims 1 to 102 are pending in the instant application.
- 2) Claims 86 to 102 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.
- 3) Claim 14 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species.

Election was made **without** traverse in the correspondence filed 05 March of 2004. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

- 4) The table presented in Figure 17B of the instant application does not comply with 37 C.F.R. 1.52 (b) with respect to font size. 37 C.F.R. 1.52 (b) states that:

“ Except for drawings, the application papers (specification, including claims, abstract, oath or declaration, and papers as provided for in this part) and also papers subsequently filed, must have each page plainly written on only one side of a sheet of paper, with the claim or claims commencing on a separate sheet and the abstract commencing on a separate sheet. See §§ 1.72(b) and 1.75(h). The sheets of paper must be the same size and either 21.0 cm. by 29.7 cm. (DIN size A4) or 21.6 cm. by 27.9 cm. (8 ½ by 11 inches). Each sheet must include a top margin of at least 2.0 cm. (¾ inch), a left side margin of at least 2.5 cm. (1 inch), a right side margin of at least 2.0 cm. (¾ inch), and a bottom margin of at least 2.0 cm. (¾ inch), and no holes should be made in the sheets as submitted. The lines of the specification, and any amendments to the specification, must be 1 ½ or double spaced. The pages of the specification including claims and abstract must be numbered consecutively, starting with 1, the numbers being centrally located above or preferably, below, the text. See § 1.84 for drawings.

37 C.F.R. 1.58 (c) states that:

Chemical and mathematical formulae and tables must be presented in compliance with § 1.52(a) and (b), except that chemical and mathematical formulae or tables may be placed in a landscape

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orientation if they cannot be presented satisfactorily in a portrait orientation. Typewritten characters used in such formulae and tables must be chosen from a block (nonscript) type font or lettering style having capital letters which are at least 0.21 cm. (0.08 inch) high (e.g., elite type). A space at least 0.64 cm. (1/4 inch) high should be provided between complex formulae and tables and the text. Tables should have the lines and columns of data closely spaced to conserve space, consistent with a high degree of legibility.

Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5) Claims 1 to 11 and 15 to 85 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims encompass subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims. These claims require a polynucleotide encoding "a mutant CNG channel comprising at least one mutation that makes the channel more sensitive to cAMP than a channel that does not comprise the mutation". It is noted that the claimed combination of a host cell expressing a heterologous G protein-coupled receptor and a heterologous cyclic nucleotide gated channel is not novel because this combination was described in Figure 3 of the Ballyk et al. patent publication (WO 98/58074, 23Dec. 1998, cited by Applicant). Therefore, the mutant GNC channel appears to be the distinguishing element of the

claimed invention. The instant specification, however, does not describe the genus of molecules encompassed by the limitation "a mutant CNG channel comprising at least one mutation that makes the channel more sensitive to cAMP than a channel that does not comprise the mutation". Whereas this limitation encompasses an almost unlimited number of CNG channels having mutations that are wholly unrelated structurally modifications, the instant specification only describes three specific mutations to a single GNC channel that provide the required functionality of increased sensitivity. In the decision of *The Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d 1398 (CAFC 1997), the court held that:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

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The instant specification does not provide a structural formula which is definitive of all CNG channel mutants having the required sensitivity by employing "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. That single CGN channel protein whose modification is described in the instant specification does not reasonably constitute a representative number of species within the genus of proteins encompassed by the limitation "a mutant CNG channel comprising at least one mutation that makes the channel more sensitive to cAMP than a channel that does not comprise the mutation".

Further, the instant specification does not provide the guidance needed to alter the particular CGN channel described therein (SEQ ID NO:2) at amino acid positions other than those three which have been identified with any reasonable expectation that different modifications will produce the desired result, and it is completely devoid of guidance in the production of an altered CGN channel having an amino acid sequence other than SEQ ID NO:2. There is absolutely no information provided about the identity of those residues in any CGN channel amino acid sequence other than SEQ ID NO:2 whose modification will produce the desired sensitivity or about the identity of alternate residues within SEQ ID NO:2 whose modification will produced the required result. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must

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bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Because one of ordinary skill in the art can not follow the guidance provided by the instant specification and alter a naturally occurring CGN channel protein and predict, "by resort to known scientific law", if a particular modification is going to increase the sensitivity of that CGN channel protein to cAMP relative to an unmodified CGN channel, the instant specification is not enabling for the full scope of these claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6) Claims 1 to 9 12, 13, 15 to 27, 22 to 49, 54 to 62, 64 to 70 and 76 to 85 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by the Ballyk et al. patent publication (WO 98/58074, 23Dec. 1998, cited by Applicant). The Ballyk et al. reference essentially described every element of the instant claims in the context in which they are claimed. The text in lines 15 to 24 on page 2 of Ballyk et al. expressly taught the production of a recombinant cell expressing a heterologous "cyclic nucleotide gated channel" (CNG channel) and "a G-protein coupled receptor" (GPCR). The text in lines 29 to 31 on page 6 taught that the CNC channels include "heterodimeric CNG

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channels that incorporate both alpha and beta subunits". The text in line 5 on page 10 taught Gi coupled GPCRs, the text in line 16 on page 11 taught chimeric G proteins, and the following paragraph taught the use of promiscuous G proteins in the disclosed cell and the assay based thereon. The text in line 7 on page 11 taught chimeric GPCRs, which would be encompassed by the limitations "mutated" and "truncated". The text on page 13 taught that the recombinant polynucleotides of that system could be transient, stable or genomic. Claims 12 and 13 recite a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, encoding the amino acid sequence of SEQ ID NO:2. This nucleic acid was described in the Dhallan et al. publication (Nature 374:184-187, 1990, cited by Applicant) and specifically employed by Ballyk et al. in the capacity claimed by Applicant, as indicated by the text at the top of page 18 of that patent publication. Further, the working examples of this publication taught the measurement of calcium flux by employing cells adherent to 96-well plates and measuring the uptake of calcium by measuring changes in the fluorescent dye Fura Red-AM with a Fluoroskan. Each of the limitations of the instant claims was either explicitly or implicitly met by the Ballyk et al. publication.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7) Claims 28 to 32, 49 to 53, 63 and 71 to 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Ballyk et al. patent publication (WO 98/58074, 23

Dec. 1998, cited above). These claims differ from those above because they recite alternate methods of measuring CNG channel-mediated ion flux in a cell or cell membrane. All of the methods recited in these claims were old and well known methods of measuring CNG channel-mediated ion flux before the time of the instant invention, as evidenced by the text on pages 22 to 24 of the instant specification. Because the Ballyk et al. reference expressly taught the need to measure CNG channel-mediated ion flux in the system described therein, one of ordinary skill in the art would have found it prima facie obvious to have employed any of those well known methods of measuring that parameter in the assay of Ballyk et al. prior to the time that the instant invention was made.

8) Claims 1 to 13 and 15 to 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ballyk et al. patent publication (WO 98/58074, 23 Dec. 1998) in view of the Scott et al. publication (Biochemistry 37:17239-17252, 1998, cited by Applicant). In so far as these claims encompass a cell and process that employ "a mutant CNG channel comprising at least one mutation that makes the channel more sensitive to cAMP than a channel that does not comprise the mutation" the text at the top of page 7 of Ballyk et al. expressly taught the use of "altered" CNG channels in the invention described therein. Further, the Scott et al. publication described a specific mutant of a CNG channel whose "cAMP-activated currents were enhanced 8-12-fold" relative to the parental protein from which it was derived. An artisan of ordinary skill in the art of receptor biology would have found it prima-facie obvious to have incorporated the

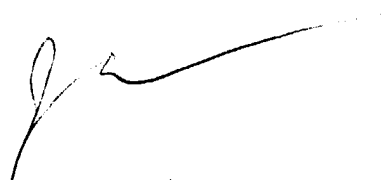
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mutant CNG gated ion channel protein of Scot et al. into the cell and assay of Ballyk et al. to increase the sensitivity of that system.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kunz Gary can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



JOHN D. ULM
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